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An Evaluation of the Potential for Use of Existing Exposure Software (or Software Currently Under Development) in a Tiered Approach to the Assessment of Exposures and Risks to Children

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1.0 Introduction

Children[1] have been identified as a subpopulation of concern for the evaluation of potential risks from chemicals. Tiered approaches to exposure assessments have been often used in regulatory assessment of different populations' exposures to chemicals. The goal of a tiered approach for exposure assessment is to begin with less complex, default-driven, screening methods and to proceed, when necessary, to more complex, data-driven, chemical- and scenario-specific methods that reduce the uncertainty in estimates of exposure. Currently there are a wide number of software packages available, or under development, that can assist in various tiers of a children's exposure assessment.

This paper begins with a brief review of the critical issues in the evaluation of children's exposures to chemicals (Section 2.0). The paper then presents a review of the exposure software (Section 3.0) and evaluates their potential for use at various points in a tiered evaluation (Section 4.0).

2.0 Children's Exposure to Chemicals

Concern for exposure to children has long been a focus for regulatory programs. EPA's Office of Drinking Water in the mid-1980s routinely evaluated exposure from oral ingestion of tapwater for both adults and children (NAS, 1977; EPA, 1985). EPA's Office of Solid Waste has focused on pica behavior in children as the primary concern for assessing risks from soil contamination at hazardous waste sites (EPA, 1989). EPA's Office of Pesticide Programs focuses on children's dermal and non-dietary oral ingestion routes when evaluating residential exposures to pesticides (EPA, 1997, 1999, and 2001). In addition, the Office of Pesticide Programs requires a separate assessment of children's dietary exposures to pesticides.

Based on the exposure assessments required by these programs and other publications (ILSI, 1992) children are generally believed to receive higher doses than adults from the following sources and routes of exposure. In addition, these routes are believed to be the most important for characterizing children's total exposures to chemicals.

1. Children consume more food and tapwater on a body weight basis than adults do. As a result, they will receive higher doses of substances that occur in food and tapwater.
2. Children's diets differ from those of adults. Infants consume breast milk and formula. As a result, children's exposures will differ from those of adults.
3. Children's inhalation rates are higher on a body weight basis than adults are. As a result, they will receive higher doses of substances that occur in air.

[1] Here and throughout this paper we use the term children to include the developing fetus, infants, toddlers, school-aged children, and teenagers.

4. Children spend more time closer to the floor. As a result, their breathing zones will be lower than adults' zones.
5. Children spend more time at home than adults.
6. Children place their hands and other objects in their mouth more frequently than adults do. As a result, they receive higher doses from contact with chemicals that occur on surfaces in the home and other environments (day care centers) where children spend large amounts of time.
7. Children consume soil and other substances at higher amounts than adults do. This consumption may be intentional (pica) or incidental (as result of other behaviors such as crawling, hand to mouth events, playing in dirt, etc.).
8. Children have higher dermal exposures because the higher ratio of surface area to body weights. As a result, doses from dermal contact of contaminants on surfaces or in water will result in higher exposures on a body weight basis.
9. Children spend more in certain institutions (day care, kindergarten, and school) than adults do.

The above findings suggest that an evaluation of exposure to children should include the ability to characterize exposures from the following sources:

1. Chemicals in food, tapwater, and breast milk,
2. Chemicals that occur in the soils or vegetation (grass or leaves) around residences and institutions (schools and day care),
3. Chemicals that occur on surfaces (floors, accessible surfaces of furniture, toys, clothing, and bedding),
4. Chemicals that occur in indoor air (from both local and distant sources) in residences and other institutions (child care centers and schools).

The assessment of children’s exposures must include dose rates that occur as a result of ingestion (both dietary and non-dietary), dermal contact, and inhalation.

3.0 Exposure Software Currently Available or Under Development

In preparing this report we reviewed the exposure assessment software packages that are currently available, or currently under development, for the performance of exposure assessment. Table 1 presents a list of the major software packages that have been developed and are currently in use or are actively being developed and will be available within the next few years. The most important packages are summarized in this section. Data for these summaries were taken from user's guides, publications, and other published descriptions of the models (Muhilan et al., 2001).

The exposure software packages can be divided into six categories:

1. Models of Consumer Product Related Exposures
2. Models of Site-Related (Industrial or Hazardous Waste Site) Exposures
3. Models of Indoor and Ambient Air Levels
4. Dietary Exposure Models

5. Aggregate exposure software
6. Libraries of Models and/or Datasets

These categories reflect the different type(s) of exposure that software packages were designed to characterize and the regulatory framework in which they were developed. The following is a description of the major software packages/programs by category.

1. Models of Consumer Product Related Exposures

These models were developed to address exposure from the use of consumer products in the home. The models have focused on inhalation and dermal routes of exposure that occur during and subsequent to the use of a product. While not listed here, European Union System for the Evaluation of Substances (EUSES) also belong in this class of software.

CONsumer EXPOsure Model (CONSEXPO-3)

CONSEXPO 3.0 is the most recent version of a multi-route, single-chemical modeling tool for assessing human exposure to chemicals emitted from consumer products. The exposure routes include inhalation, dermal, and oral. For each route of exposure, a number of exposure and uptake models are included. CONSEXPO 3.0 is a 32-bit application for the Windows® environment (Windows95®, 98, ME, or NT)

CONSEXPO is designed to assist in the evaluation of exposure from consumer products. The software includes a number of modeling options that vary from screening models to models that are intended to realistically predict actual exposures and doses. CONSEXPO is based on a modeling framework developed by Van Veen (1995; 1996) to evaluate contact, exposure and uptake of chemicals emitted by consumer products. In this framework, exposure is defined as the concentration of a chemical compound in the medium touching the body. Uptake includes both the intake rate of the contaminated medium and the uptake rate of the compound by the body.

CONSEXPO focuses on non-professional indoor use of consumer products. It provides two tools; a set of algorithms for the calculation of exposure and a database of model inputs. The models form the core of the program as they provide the exposure and dose estimates. The database is set up to provide input to the models. The database is organized by product categories. After the user selects a product category, the database provides default parameter values to the models.

The doses received from dermal contact are modeled in two steps; dermal exposure (or dermal loading) and dermal absorption. The goal of the dermal loading models is to describe the time course of the contaminant at the boundary of the skin that occurs as a result of an exposure event(s).

Because of the wide range of exposures associated with consumer products, there are five dermal loading scenarios defined, and one scenario to model dermal exposure to airborne compounds. The five dermal loading scenarios are:

- Fixed volume scenario assumes that the product is well mixed;
- Diffusion in product scenario assumes that the product is not well mixed and transport of a chemical compound takes place by means of diffusion;
- Migration to skin, scenario assumes that dermal exposure as a result of migration of product to the skin;
- Transfer coefficient and contact rate scenarios that are similar to the dermal models used in the EPA's residential SOPs.

Note that some of these models require a consideration of dermal absorption as a factor that influences the time course of a contaminant concentration at the skin boundary.

Dermal absorption is modeled using either a simple "absorbed fraction" or by use of one of two diffusion models. The first diffusion model uses the concentration difference between the product and the blood in the skin. The second an existing model, SKINPERM, makes the simplifying assumption that the concentration in blood is always zero. In both models, the uptake is proportional to the concentration difference, and skin permeability. The skin permeability coefficient can be estimated by any one of six empirical formulas based on the compound's log K_{OW} and the molecular weight.

CONSEXPO does not address oral exposure from agricultural sources of contamination. The model does consider exposures that occur from the use of products including certain food-mediated exposures. CONSEXPO has five models of oral exposure from products. These are as follows:

1. Ingestion of products used in and around the mouth (toothpaste, mouthwash, etc.);
2. Ingestion of aerosols or particulates, that are inhaled and deposited in the nasal-pharyngeal tract;
3. Ingestion of residues by the surface-to-hand-to-mouth pathway;
4. Placing objects in the mouth (leaching from product); and
5. Leaching of contaminants into food items that are subsequently consumed (food packaging or containers).

Oral absorption of ingested contaminants can be modeled based on a simple absorption fraction or by a "tube model of diffusion". The diffusion model can incorporate matrix effects where the contaminant is absorbed as part of a solid.

CONSEXPO has an option that allows the user to input certain input parameters in the form of distributions rather than point estimates, enabling Monte Carlo simulation and sensitivity analysis.

E-FAST

The Exposure and Fate Assessment Screening Tool (E-FAST) was developed by Versar, Inc. for the United States Environmental Protection Agency, Office of Pollution Prevention and Toxics. E-FAST provides screening-level estimates of the concentrations of chemicals released to air, surface water, landfills, and from consumer products. Estimates provided are potential inhalation, dermal and ingestion dose rates resulting from these releases. Modeled estimates of concentrations and doses are designed to reasonably overestimate exposures, for use in screening level assessment. E-FAST is the modeling successor to a number of consumer models including SEAS, Facsearch (SIDS), PDM3, FLUSH, DERMAL, and SCIES**.** EFAST is a stand-alone program that is run on IBM-compatible PC Windows95®, Windows98®, or WindowsNT®.

E-FAST, like most consumer models, defines the population modeled as the exposed population. The model does not investigate variation in dose in the exposed population or the uncertainty in the estimate. The basis estimate of exposure is the potential dose received from a single event. Using conservative assumptions of the frequency of events, the model estimates the average dose rate that occurs over longer periods of time. E-FAST estimates the levels in the environment associated with the use of certain classes of products and the doses that occur from the consumption of tapwater and contaminated fish.

Dermal exposures from consumer products are evaluated using a film-thickness approach. This approach defines the potential dermal dose as the amount contained in a thin film on the skin. The model also evaluates dermal absorption using a permeability coefficient. Inhalation exposure is estimated using a deterministic mass balance calculation. Indoor air in a home is modeled using a two-zone model where the first zone is the room where the product is used and the second zone is the remainder of the home. The model does not consider sinks. Air emissions are modeled using a variety of emission models depending on the exposure scenario chosen.

The software contains a series of pre-defined scenarios that facilitate the evaluation of consumer products. These include:

- General Purpose Cleaner (dermal and inhalation)
- Interior Latex Paint (dermal and inhalation)
- Fabric Protector (inhalation)
- Aerosol Paint (inhalation)
- Liquid Laundry Detergent (inhalation)
- Liquid Laundry Detergent (dermal)
- Solid Air Freshener (inhalation)
- Bar Soap (dermal)
- Used Motor Oil (dermal)
- User Defined

PROBABILISTIC METHODOLOGY FOR IMPROVING SOLVENT EXPOSURE ASSESSMENTS PROMISE©

PROMISE© is an ongoing modeling project (Version 7, released June, 2001) by Silken, Inc., for the Solvents Council of the American Chemistry Council. The software is designed to evaluate exposures and doses from single and multiple uses of products that contain volatile solvents (adhesives, nail polish, paints, floor cleaners, etc.), from activities surrounding the use of large volumes of solvents (open drums or open tanks), or from spills. The model can be used to investigate products used in the workplace and the home.

PROMISE© can calculate multi-route exposures from dermal, inhalation (indoor or outdoors), and/or ingestion routes of solvent exposure. The distribution of the dose can be evaluated and compared for various exposure pathways, alternative exposure and uptake models, and will allow a tiered analysis of exposure. PROMISE© is written FORTRAN and is designed to run on PCs in the Windows® environment (Windows95®, Windows98®, or WindowsNT®).

PROMISE© is not a population model. It defines the individuals modeled as users or residents where a solvent product is being used. PROMISE© is a model of the interindividual variation in the doses received in the exposed population.

PROMISE©'s focus is the derivation of dose rates that occur over one day to a lifetime. Estimates of exposure that occur over periods longer than one day assume a regular pattern of exposure of one or more exposure events that can be specified by the user. Each type of exposure event in an individual's exposure history is assumed to be identical.

PROMISE© has algorithms that describe the movement of solvent for an applied product, solvent container, or from a spill. The source models offered in PROMISE© are labeled constant concentration, source and ventilation, pure-substance evaporation, "open-can" evaporation, and wall or floor liquid application and evaporation. The program's algorithms model the release of solvent from mixtures that change over time. The model also allows the consideration of the use of multiple products on a surface over time. The equations track the time course of the solvent's concentration in air over time. The model also allows a limited modeling of the receptor's characteristics and how they influence dose. PROMISE© includes multiple alternative models for exposure and uptake for each route.

PROMISE© makes use of a proprietary Monte Carlo model, DISGEN©. This model can be used to model variation in dose or the uncertainty in dose depending on the nature of the distributions entered into the model. PROMISE© is one of the few models identified that address the workplace as well as the home. The model's strengths are the clearly documented algorithms for solvent release from products and for dermal uptake.

2. Models of Site-Related (Industrial or Hazardous Waste Site) Exposures

These models were developed to facilitate the evaluation of exposures from point sources such as specific industrial sites, hazardous-waste sites, and other local sources of emissions. The models are usually multimedia, tracking contaminants through various exposure pathways. However, all the pathways are related back to a single local source. Many of the packages are based on EPA's Risk Assessment Guidance for Superfund Sites (EPA, 1989).

These models generally have a strong focus on exposure to children. They will be useful for the evaluation of exposure to local environmental sources such as contaminated soil and air.

API DSS

The American Petroleum Institute Decision Support System (API DSS) was developed to assist environmental professionals in estimating human exposure and risks from contaminated sites. It can be used to approximate site-specific risks, identify the need for site remediation, develop and negotiate site-specific cleanup levels with regulatory agencies, and evaluate the parameter of variability and uncertainty on estimated risk. Four modules make up API DSS Version 2.0 including, the Development of Risk module, the Receptor Point Concentration module, the Chemical Intake and Risk Calculation module, and the Risk Presentation module. The Chemical Intake and Risk Calculation module uses the estimated dose and chemical-specific toxicity to estimate carcinogenic risk and non-carcinogenic hazard index and can be used in either deterministic or Monte Carlo simulation modes. The results of the analysis can be viewed in tabular and graphical format by the Risk Presentation module. The relevant pathways evaluated by the models include vapor intrusion (from soil) into homes, volatilized chemicals from bathroom showers, soil ingestion, and ingestion of food and water.

CalTOX

CalTOX was developed to assist the Department of Toxic Substances Control, within the California Environmental Protection Agency, in health risk assessments. It is comprised of a set of spreadsheet models and databases, which can be used to assess human exposure and define soil clean-up levels at uncontrolled hazardous waste sites. The relevant pathways evaluated by CalTOX include contaminated soils and the contamination of adjacent air, surface water, sediments, and ground water. It is composed of various modeling components including a multimedia transport and transformation model, exposure scenario models, and add-ins to quantify and reduce uncertainty and variability. The multimedia transport and transformation model can be used to evaluate time-varying concentrations of contaminants introduced initially into the soil layers and contaminants released continuously into the air or water. CalTOX examines how chemical and landscape properties impact both the ultimate route and quantity of human contact. To estimate average daily potential doses within a human population the multimedia, multiple pathway exposure models are used in the CalTOX model. Twenty-three exposure pathways are contained within the exposure models. In the exposure assessment, contaminant concentrations in the multimedia model compartments are related to contaminant concentrations in the media with which a human population has contact including personal air, tap water, foods, household dusts, and soils.

CalTOX is run using the programs Excel and the Excel add-in program Crystal Ball. The program consists of two linked spreadsheets one models fate and transport the second the dose from exposures.

CalTOX is a source model and defines the model population as those individuals who are exposed to one or more waste-related sources of exposure. The model can evaluate the impact of interindividual variation of input parameters on dose to the exposed individuals. CalTOX can evaluate long-term exposures (70 years). The model is also designed to track changes in source terms over time.

CalTOX evaluates exposures by a large number of pathways including the following:

Inhalation

- Inhalation of gases and particles in outdoor air;
- Inhalation of gases and particles transferred from outdoor air to indoor air;
- Inhalation of soil vapors that migrate to indoor air;
- Inhalation of soil particles transferred to indoor air;
- Indoor inhalation of contaminants transferred from tap water

Ingestion

- Ingestion of fruits, vegetables, and grains contaminated by transfer of atmospheric chemicals to plant tissues;
- Ingestion of meat, milk, and eggs contaminated by transfer of contaminants from air to plants to animals;
- Ingestion of meat, milk, and eggs contaminated through inhalation by animals
- Human soil ingestion;
- Ingestion of fruits, vegetables, and grains contaminated by transfer from soil;
- Ingestion of meat, milk, and eggs contaminated by transfer from soil to plants to animals;
- Ingestion of meat, milk, and eggs contaminated through soil ingestion by animals;
- Ingestion of mother's milk;
- Ingestion of tap water;
- Ingestion of irrigated fruits, vegetables, and grains;
- Ingestion of meat, milk, and eggs from animals consuming contaminated water;
- Ingestion of fish and seafood;
- Ingestion of surface water during swimming or other water recreation;
- Ingestion of mother's milk

Dermal contact

- Dermal contact with soil;
- Dermal contact with tapwater in baths and showers; and
- Dermal contact while swimming.

Exposures are estimated using standard exposure equations for waste sites that have been modified to account for the effect of mass balance (EPA, 1989)

CalTOX focuses on the exposed individual. Entering distributions into the equations can allow the determination of the variation, uncertainty, or combination of uncertainty and variation in exposure in the population of exposed individuals.

MEPAS

The multimedia environmental pollutant assessment system (MEPAS) was developed by Pacific Northwest Laboratory of Battelle for the U.S. Department of Energy (DOE). MEPAS is a set of codes developed to provide integrated risk information for hazardous, radioactive, and mixed-waste sites. MEPAS couples models of contaminant release, migration, and fate for environmental media with dose rate models based on exposure routes and health consequences for radiological and non-radiological carcinogens and non-carcinogens. Contaminant transport media includes groundwater, overland flow, surface water, air, and food pathways. Human exposure routes include ingestion, inhalation, dermal contact, and external dose. MEPAS provides an overall risk assessment by looking at all pathways and computing aggregate risk to humans from a particular site.

RISK*ASSISTANT

RISK*ASSISTANT was developed by Hampshire Research Institute. It provides information on hazard, exposure, and risk, and allows flexibility to tailor the assessment to local sites. The exposure pathways that can be assessed include air, surface water, ground water, soil, sediment, and food. RISK ASSISTANT allows the choice of chemical and concentration data sets, alternative populations, exposure scenario factors, and toxicity data sets. Risks can be calculated for single scenarios or multiple scenarios. Sensitivity analyses can be performed to determine the effect of exposure variables on risk estimates.

SMARTRISK

SmartRISK is a multi-chemical, multi-pathway human health risk assessment modeling program. Pick lists with media, chemicals, and exposure routes are used to build exposure models. SmartRISK uses this information combined with exposure point concentrations and data in user defined default databases to evaluate exposure and calculate risks. Four different exposure scenarios can be evaluated at one time for reasonable maximum exposed (RME) and alternative exposed populations. All calculations are deterministic. Risk reports created by SmartRISK can be transported to a spreadsheet to perform Monte Carlo Simulation using Crystal Ball or @RISK.

4. Models of Indoor and Ambient Air Levels

These models are predominantly source models and focus on the estimation of the temporal and spatial variation of air concentrations in indoor environments. Models rely upon mass balance equations and fate and transport models.

This category of models includes a variety of models. Fate and transport models (TOXLT/TOXST) model the release of contaminates from local sources and the resulting air concentrations at near by residences. Other models largely focus on the release of airborne contaminates to indoor air and the resulting indoor air levels (IXAQ, CONTAM, MCCEM, and RISK). A third type of models creates simulations of individuals who interact with different indoor microenvironments (Indirect models). Finally, the models CPEIM, TEM and TRIM attempt to address exposure from oral and dermal routes of exposure. Thus, these models should also be considered aggregate exposure models.

TOXLT/TOXST

The Toxic Modeling System Long-Term (TOXLT) was developed along with the release of the new version of the EPA's Industrial Source Complex (ISC2) Dispersion Models and the development of a tiered modeling approach for assessing the risks due to sources of hazardous air pollutants. TOXLT assists in the evaluation of the lifetime cancer risks and chronic non-cancer hazards that may result from long-term exposure to toxic air pollutants. ISCLT2 model is used to stimulate annual average pollutant concentrations, which are then used to estimate cancer risk levels or hazard index values at each user-specified receptor. These outputs presume: (1) a hypothetical individual exists at each receptor, (2) no contribution from "background" sources, and (3) pollutant contributions in a mixture are additive.

The Toxic Modeling System Short-Term (TOXST) addresses the problem of estimating expected exceedances of specified short-term health effects thresholds in individuals living near a source of continuous or intermittent toxic releases.

Multi-Chamber Concentration and Exposure Model (MCCEM)

The Multi-Chamber Concentration and Exposure Model (MCCEM) is a user-friendly computer program that estimates indoor concentrations for, and inhalation exposure to, chemicals released from products or materials used in a residence. MCCEM is intended to support EPA/OPPT in assessing inhalation exposures to new and existing chemicals in consumer products, building materials, or indoor furnishings. For each model run, time-varying indoor-air concentrations and inhalation exposure are modeled for one chemical in as many as four zones (chambers) of a residence. One exposure event (e.g., one episode of use of a consumer product) typically is modeled, from which single-event and lifetime exposure estimates are developed based on user inputs.

MCCEM is written entirely in C++ and is a stand-alone program that runs on Windows95® (and later versions of Windows®). The primary output of the model is a set of exposure measures (e.g., peak concentration, single-event dose, LADC, LADD) relating to the exposure event that has been modeled. For lifetime exposure measures such as LADC and LADD, it is assumed that the modeled exposure event occurs repeatedly throughout an individual's lifetime, at a frequency specified by the user. A time-series of indoor-air concentrations in each zone also is output from the model, in a format that can be imported readily into spreadsheet software such as Excel.

The user can choose from several types of pre-formatted emission profiles for these sources, or can enter time-varying emission rates explicitly or import them from an ASCII file. The four types of source models available in MCCEM are constant, single exponential, incremental and data entry. MCCEM currently does not include complex source models such as those for aerosols (e.g., to treat coagulation of particles in the air and subsequent size-dependent particle deposition rates), but can account for reversible and irreversible indoor sinks.

Exposure in MCCEM is the concentration to which an individual is exposed, multiplied by the inhalation rate. Both of these quantities can vary over time within the model. Exposure is calculated at each time step (30 seconds) for which concentrations are calculated by the model, and then summed over the duration of the model run to determine single-event dose. To estimate lifetime exposure measures such as LADC or LADD, MCCEM generally relies on exposure equations specified in EPA's Exposure Factors Handbook (1997a).

Three different inhalation-dose calculations are performed in MCCEM: Lifetime Average Daily Dose (LADD); Average Daily Dose (ADD); and Acute Potential Dose Rate (APDR). For LADD calculations, the averaging time is the lifetime of the individual. For the ADD calculations, the averaging time is the number of years the emitter is in the house, the same as the number of years of exposure. For the APDR calculations, an averaging time of one day is used. That is, the APDR is the highest dose over a 24-hour period during the exposure event.

Three different inhalation concentration calculations are performed in MCCEM: Lifetime Average Daily Concentration (LADC); Average Daily Concentration (ADC); and Peak Concentration (Cpeak). The peak concentration is the highest instantaneous modeled concentration during the exposure event.

MCCEM has a Monte Carlo option that allows the user to develop a range of exposure estimates by making multiple runs while varying one or more of the following parameters – infiltration rate, emission rate or sink rate – around the values entered on other input screens. With this option, each input parameter chosen by the user is treated in the form of a distribution, with a central value that represents the user's input on the corresponding screen. Four types of distributions are available for each input parameter – uniform, normal, triangular and lognormal. When Monte Carlo simulation is used, the output from MCCEM is restricted to summary statistics (e.g., peak concentration, LADC) for each trial.

Simulation Tool Kit for Indoor Air Quality and Inhalation Exposure (IAQX)

IAQX Version 1.0 consists of five stand-alone simulation programs. A general-purpose program performs multi-zone, multi-pollutant simulations and allows gas-phase chemical reactions. Other programs address VOC emissions from solvent-based indoor coating products, small-scale solvent spills, VOC emissions from diffusion-controlled homogeneous slabs, and indoor particulate matter. In addition to performing conventional IAQ simulations, which compute the time-varying concentration profile and inhalation exposure, IAQX can estimate the adequate ventilation rate when certain air quality criteria are provided by the user.

IAQX is a Windows-based simulation software package. The primary outputs of the model are concentration, inhalation exposure, and adequate ventilation rate. IAQX is intended to model exposure for a single exposure event and a single individual, but can handle multiple contaminants in a single run. There is no modeling of a population. IAQX offers a variety of source models that can address emission of chemicals from consumer products, building materials, indoor furnishings, and appliances.

The general-purpose simulation program offers 26 source models as well as 5 sink models and 2 air-filter models. It also allows gas-phase chemical reactions. The source-model groups available in this program include constant and instant sources, first-order and higher-order sources (e.g., exponential decay), solvent evaporation, dry sources, emissions from water, and time-varying indoor sources.

CONTAM

CONTAM (Dols et. al., 2000) is a computer model developed at the National Institute of Standards and Technology (NIST). CONTAM was originally developed in the 1980's, and the current version, CONTAMW 1.0, is a Windows® based implementation of early versions. CONTAM is a multizone indoor air quality and ventilation model designed to predict contaminant air concentrations and personal exposure resulting from the release of chemicals by a variety of processes.

The current version, CONTAMW 1.0, is a stand-alone program that runs under Windows95/98® or WindowsNT®. Model results can be viewed using built-in charting features for viewing airflows, concentrations and exposures. In addition, the results can be exported to comma delimited data files for import into charting and analysis programs such as Microsoft Excel. The CONTAM user interface requires the user to supply information about the building components, occupants, weather, and wind profiles.

The most sophisticated capabilities of the model are in the building component definitions and simulation of contaminant emissions and movement. The building component modules allow representation of the following:

- Walls, floors and ceilings, including airflow paths and cracks or leakage areas;
- Levels (or floors) of a building;

- Zones or volumes of uniform temperature and contaminant concentrations;
- Mechanical air-handling equipment, including ducts operating schedules; and
- Contaminant emission and sink models.

COMTAM also provides models for several special cases of leakage, such as doorways and chimneys, and provides methods for representing duct flow and the operation of fans. Occupant exposure is estimated by providing CONTAM with schedules of locations and breathing rates. Weather and wind effects are represented by schedules. CONTAM then accounts for the effect of wind and temperature on ventilation using fundamental equations for describing temperature and pressure driven airflow across openings in the building envelope.

CONTAM is not a population exposure model, and therefore is not ideally suited to estimating population-based exposures. Individual occupant exposure can be estimated by defining individual location and breathing schedules, but variations in the population can only be represented on an individual case basis. The duration of time is user defined, with all inputs such as emission, wind, and occupancy schedules defined over the desired duration.

The available emission models are constant, pressure driven, decaying, and burst release. CONTAM also provides the boundary layer diffusion sink model. These models may be defined in a global manner, representing emissions from building materials, such as emissions from a newly painted room. The user may also define occupant emission rates – or contaminants released by the occupant at the current occupant location.

CONTAM provides for the estimate of inhalation exposure by using the inhalation rate schedule in combination with predicted air concentrations from model predictions. The model also provides for an inhalation multiplier, a constant multiplier applied to the estimated inhalation exposure, meant to allow the user a means for predicting dose. No models are available for predicting other routes of exposure.

CONTAM solves the system of contaminant mass-balance ordinary differential equations (ODEs) by a user-selected choice of three solution techniques: (1) a direct skyline algorithm; (2) an iterative bi-conjugate gradient algorithm; or (3) an iterative successive over-relaxation algorithm. Contaminant emissions, sinks, pressure, and airflow relationships are described using the appropriate equations within the system ODEs.

RISK

RISK is the third in a series of indoor air quality models developed by the Indoor Environment Management Branch of the USEPA National Risk Management Research Laboratory. RISK was designed using the concepts of buildings and scenarios. The fixed information about a building, number of rooms, room dimensions, and arrangement of the rooms is contained in a building file. The changing information – sources, sinks, air exchange, room-to-room flows, etc. – is contained in scenario files. The steps in using the model are: (1) define the building; (2) save the building information to a file; (3) define the scenario; (4) save the scenario to disk; and (5) run the model. RISK provides a wide range of graphical and tabular outputs of the results of the calculations. Summary outputs of risk and exposure are provided in tabular form. Full risk, exposure, and concentration outputs are also provided in tabular form. The tabular output is supplemented by graphs of concentration and exposure versus time. The calculated results can also be saved to disk for later analysis.

RISK can model durations ranging from one day or shorter to multiple years.

RISK can accommodate sources such as consumer products, building materials, indoor furnishings and appliances. Source models available in RISK include exponential decay models, mass transfer models, empirical models for latex paint, and on/off (constant emission rate when on) models. The model also can account for reversible and irreversible indoor sinks.

California Population Indoor Exposure Model (CPIEM)

The California Population Indoor Exposure Model (CPIEM) combines indoor-air concentration distributions with Californians' location/activity profiles to produce exposure/dose distributions for different types of indoor environments. This function is achieved through a Monte Carlo simulation whereby location/activity profiles from prior surveys by the California Air Resources Board are combined with distributions of airborne concentrations for various environments (e.g., residences, schools, office buildings). For many compounds, the concentration data for a given type of environment are either limited or nonexistent. Consequently, the model also has the capability to estimate indoor-air concentration distributions based on distributional information for mass-balance parameters such as emission rates, building volumes and air exchange rates.

CPIEM is written in QuickBASIC® for the DOS platform. The primary outputs of the model are summary statistics and accompanying graphs describing the concentration, exposure or dose distribution estimated by the model.

For each trial or iteration of the model, an activity profile is sampled from a set of about 3,000 such profiles. The user can select from subgroups of activity profiles defined by factors such as age, gender, primary activity (e.g., work, school, retired), geography and time of year. The modeling duration for each trial is 24 hours.

Indoor-air concentrations can be modeled in CPIEM for a variety of indoor sources including consumer products, building materials, furnishings and combustion appliances. Sources are categorized in CPIEM as frequent (e.g., tobacco smoking, showering), episodic (e.g., painting, wood burning), and long-term (e.g., range pilot lights, building materials), with a series of input screens keyed to each category.

The model estimates distributions for inhalation exposure and potential inhaled dose. Inhalation exposure is the time-integrated concentration encountered by an individual while in an indoor environment. Potential inhaled dose is the product of the time-integrated concentration and the individual's breathing rate (i.e., amount of air inhaled per unit time while in the environment). The 24-hour, time-integrated inhalation “exposure” in CPIEM is the sum of time-integrated air concentrations encountered by an individual in the course of his/her sequential visits to different environments throughout the day. Within each environment, the time-integrated concentration is simply the product of the sampled (average) air concentration multiplied by the time duration in the environment. Similarly, within each environment the inhalation dose is the product of the concentration times the duration times the breathing rate while in the environment.

Monte Carlo simulation is an integral part of the CPIEM software. The statistical stability of various estimates produced by the model (e.g., mean exposure/dose and various percentiles of the exposure/dose distribution) can be assessed by making repeated model runs with all inputs constant except the user-selectable random number seed.

The Total Exposure Model (TEM)

The Total Exposure Model (TEM) is a computer model that has been developed with support from the USEPA and the US Air Force. The model is a descendent of a model named MAVRIQ (Model for the Analysis of Volatiles and Indoor Air Quality, Wilkes et. al., 1992, Wilkes et. al., 1996). TEM (Wilkes, 1998) is designed to predict the exposure and dose to an individual resulting from use of a contaminated water supply by modeling the fundamental physical and chemical processes that occur during interaction between the contaminated media (in this case water and air) and the exposed individual. The dermal, inhalation, and ingestion calculations are separately maintained to allow a comparison of their respective effects. The integrated model combines emission and fate and transport submodels to estimate resultant human exposure to an individual or population group. The model also estimates body burden (dose to the individual's blood supply). The model also contains an integrated simplified physiologically based pharmacokinetic (PBPK) model and is compatible with a comprehensive PBPK model (ERDEM, Exposure Related Dose Estimating Model). The feasibility of applying TEM to predict exposure and uptake to chloroform based on field data has been demonstrated. (Wilkes and Nuckols, 2000, Lynberg et. al., 2000).

Earlier versions of the model were developed primarily as research tools, but the current version has been developed into a user-friendly tool meant to assist in both population based and individual based exposure assessments. TEM uses Monte Carlo techniques to merge activity pattern data with stochastic or deterministic multiroute exposure models (ingestion, inhalation, and dermal contact) to estimate distributions of exposure of the population to drinking water constituents.

TEM is a stand-alone program developed in C/C++ that runs under Windows95® or later. Model results are stored in an Access database. The model outputs airborne concentrations, personal concentrations, exposures, absorbed dose, and individual target organ concentrations, which can be viewed using built-in charting features. More detailed information about the model inputs, sampled activity patterns, simulated water uses, and a variety of other simulation information is contained in the Access database. In addition, the results can be exported into charting and analysis programs such as Microsoft Excel.

TEM is developed to function either as an individual case study model or for estimating population-based exposures. When applied to an individual case study, the user specifies the exact scenario of activities being studied. The model can also be applied in a population mode with user-selected populations and user-defined population characteristics. TEM combines stochastic representation of exposure-related behavior with deterministic calculations of emissions, air concentrations, exposures, and doses. When applied in a population mode, the user specifies the characteristics of each population group as made available by the activity pattern survey. For example, NHAPS provides characteristics such as age, gender, employment, and location in the U.S. Subsequently, TEM can sample activity patterns from NHAPS meeting the desired characteristics and use the sampled activity patterns as a basis for predicting the distribution of exposures to the specified population. Other input behavioral variables, such as source use behavior, may be represented stochastically as a Poisson process for event occurrence and as a lognormal distribution for event duration.

The model implements a number of algorithms to allow stochastic representation of population behavior. The model allows the user to define airflow patterns that respond to user behavior (e.g., when a user takes a shower and the bathroom door is closed, a set of airflows specific to that user behavior may be automatically invoked by the model).

The model simulates the user defined time period for an individual case study and a 24- hour period for a population-based exposure assessment.

TEM is designed to represent emissions from a domestic water supply during normal household water uses. As such, TEM is ideally suited for evaluating exposure and dose to any waterborne contaminant. TEM contains a variety of emission models specifically developed to address the release of contaminants from water use appliances in the home. The models are fundamental mass-transfer models developed based on laboratory experiments and the two-film mass transfer theory (Whitman, 1923). Specific water-use emission models are provided in TEM to represent releases from showers, baths, clothes washers, dishwashers, faucets, and toilets. In addition, a generic plug flow model and a completely mixed flow models (CMFM) are provided.

In addition to the emissions specific to waterborne contaminants, TEM also contains general emission models for release of contaminants to the air, including constant, decaying exponential, and burst release. A reversible sink model is also provided.

TEM evaluates exposure and dose to waterborne contaminants that are ingested. Algorithms are provided for stochastically representing ingestion of contaminated drinking water in accordance with user input values for quantity and frequency of consumption. These parameters are also being analyzed based on information contained in the CSFII data (EPA, 2000), and these data will be incorporated into the model.

The primary route of exposure for volatile waterborne constituents is the inhalation route. TEM evaluates this exposure by modeling the release of the contaminant during water uses by the aforementioned emission models, the fate and transport of the contaminants, the activities and locations of the occupants, and the physiological and chemical processes leading to uptake into the body. Calculations are preformed utilizing an equilibrium lung model to estimate the mass transferred from the inhaled air into the bloodstream.

The dermal exposure and uptake is also estimated based on skin diffusion mass transfer models. The membrane model (Cleek and Bunge, 1993, Wilkes, 1998) is used for estimating the mass transfer across the skin. A simpler, steady state model is also provided (Wilkes, 1998).

TEM solves the system of contaminant mass-balance ordinary differential equations (ODEs) by the fourth-order Runge Kutta method (also known as the Kutta-Simpson formula) for temporal integration. Contaminant emissions, sinks, pressure, and airflow relationships are described using the appropriate equations within the system ODEs.

TEM uses databases to provide information necessary for modeling population based exposure behavior. The databases currently linked to TEM or databases used to implement TEM include the following:

Ingestion: The 1994-96 USDA's Continuing Survey of Food Intake by Individuals (CSFII) is the most recent and comprehensive consumption database available. The EPA report, Estimated Per Capita Water Ingestion in the United States (EPA, 2000), explains the details of the study and presents the results

Human activity patterns: National Human Activity Pattern Survey - NHAPS is the largest and most current (1992-1994) human activity pattern data set available. Data for 9386 respondents in the 48 contiguous United States were collected via minute-by-minute 24-hour diaries. Detailed data were collected for a maximum of 82 possible locations and a maximum of 92 activities. In addition, demographic data was collected for each respondent (gender, age, education, week day/weekend, race, census region, race etc.). Advantages of the NHAPS data set are that it is representative of the U.S. population and it has been adjusted to be balanced geographically, seasonally, and for day/time. In addition, it is representative for all ages, gender, and race. This data set has many of the attributes for constructing stochastic activity pattern models (location, duration, frequency) and it is very data rich in water-related activities including taking baths, taking showers, amount of time in the bathroom after bathing or showering, washing of hands, using dishwasher, washing dishes by hand, swimming, etc.

Water use behavior: The Residential End Uses of Water Study (REUWS) database contains water use data obtained from 1,188 volunteer households throughout North America (Mayer et. al., 1998). The REUWS study was funded by the American Water Works Association Research Foundation (AWWARF). During the period from May 1996 through March 1998, approximately

100 single-family detached homes in each of 12 different municipalities (located in California, Colorado, Oregon, Washington, Florida, Arizona, and Ontario) were outfitted with a data-logging device (Meter Master 100 EL, manufactured by Brainard Co., Burlington, NJ) attached to their household water meter (on only magnetic driven water meters). The data logger recorded the water flows at 10-second intervals for a total of four weeks (two in warm weather and two in cool weather) at each household. Following the study, the data was retrieved and analyzed by a flow trace analysis software program, called Trace Wizard, developed by Aquacraft, Inc., Boulder, CO, which disaggregated the total flows into individual end uses (i.e. toilet, shower, faucet, dishwasher, clothes washer, etc) (Mayer et al. 1998). In addition to identifying the type of water use (e.g. shower, faucet, toilet), Trace Wizard identified the event durations, volumes, peak flows, and mode measurements for each water-using event.

The Residential Energy Consumption Survey (RECS) was a nationwide survey conducted in 1997 to obtain household energy use information. The resultant RECS database contains energy usage characteristics of 5,900 residential housing units. The information was acquired through on-site personal interviews with residents; telephone interviews with rental agents of units where energy use was included in the rent; and mail questionnaires to energy suppliers to the units. The database contains information on physical characteristics of the housing units, demographic information of the residents, heating and cooling appliances used, clothes washer and dishwasher use frequency information, fuel types, and energy consumption.

Total Risk Integrated Methodology (TRIM)

TRIM is an ongoing modeling project of EPA’s Office of Air Quality Planning and Standards. The program is intended to support OAQPS action under the Clean Air Act (CAA). They include the residual risk program, delisting petitions, and the establishment of national ambient air quality standards. Air emissions can result in exposures by multiple pathways, oral and dermal, as well as inhalation. As a result, TRIM has been designed to evaluate the aggregate exposures to a single compound that occur as the result of the releases of that compound to air. The concern for risks from air pollutants ranges for acute exposures to lifetime average exposures; therefore, TRIM will evaluate exposures that occur over a wide range of durations. The model also has to be able to track the exposure and resulting dose back to sources regulated under the CAA. Therefore, TRIM is being designed to link a longitudinal aggregate exposures model to a fate and transport model.

The model is being developed in phases. APEX is one of the exposure models that are being designed for use within TRIM.Expo. This and other models are scheduled for external review and testing of in Spring/Summer 2002. EPA will be working on the ingestion component in 2002.

TRIM is being designed as a modular program designed to be run on PCs. The model has three key components:

- TRIM.fate;
- TRIM.expo; and

- TRIM risk.

TRIM.fate is designed to relate air emissions sources in specific geographic locations to levels of contaminants in air food and water at specific locations in the U.S. TRIM.expo is a longitudinal model of aggregate exposures to individuals and cohorts. TRIM.risk combine toxicity data and the output of TRIM.expo.

TRIM has a strong geographic orientation that results from the need to relate exposure and risk back to specific emission sources at specific locations. Thus, the model focuses on geographically defined study areas (census tracts, or other areas). Larger areas are built up from these units. Using this approach, the entire U.S. can be studied.

Inside the units the population can be divided based on a wide variety of demographic factors. TRIM relies on groups of individuals called cohorts, which are treated as having similar exposures. TRIM is designed to estimate exposures for all time periods from less than a day to the average dose across a lifetime.

TRIM is still under development; thus, the specific pathways that will be address in future versions are uncertain. Pathways that are under consideration include the following:
- Inhalation out of doors (ambient air levels);
- Inhalation in microenvironments (indoors, vehicles, workplaces, institutions, etc.);
- Consumption of fish;
- Tapwater consumption;
- Ingestion of soil and house dust;
- Non-ingestion tapwater pathways;
- Consumption of locally produced meat and dairy products, and
- Consumption of locally grown agricultural commodities.

In all of the pathways, the emphasis is on how these routes of exposure could be affected by release of contaminants to air. (These pathways are addressed in TRIM.fate.)
The exposures are evaluated using an “event” model. An event could be inhalation in a microenvironment or the consumption of a food item. Activity pattern data are used to define the events in a person’s life. TRIM will be based on the CHADS database.

Indirect Models

The models described below are not indoor-air models per se. Rather, they share a common feature in that total (24-hour) exposure distributions can be developed by combining distributions for microenvironment-specific concentrations with information on population activity patterns, or time spent in each microenvironment by individuals. Nearly all of these models involve use of Monte Carlo simulation techniques and began with an emphasis on estimating population exposures to airborne contaminants in outdoor air. Some have evolved to the point of including mass-balance routines to simulate concentration distributions for indoor environments.

The table below summarizes selected features of the following models:

- AirPEX (Air Pollution Exposure Model);
- BEAM (Benzene Exposure Assessment Model);
- HEM (Human Exposure Model;
- pHAP (probabilistic Hazardous Air Pollutant exposure model);
- pNEM (probabilistic NAAQS Exposure Model);
- SHAPE (Simulation of Human Activities and Pollutant Exposure);
- HAPEM (Hazardous Air Pollutant Exposure Model); and
- SCREAM (South Coast Risk and Exposure Assessment Model).

As summarized in the table, some of the models use a simplistic approach such as indoor/outdoor (I/O) ratios to estimate indoor-air concentrations, whereas others use a mass-balance framework.

Model	Contaminants	Estimation of Indoor-air Concentrations
BEAM	Benzene	
HEM	Toxic air pollutants	I/O ratios
PHAP	Hazardous air pollutants	
PNEM	O_3, CO, PM	Mass-balance model
SHAPE	CO	
HAPEM	Hazardous air pollutants	Penetration factors
SCREAM	Air toxics	I/O ratios, mass-balance model

3. Dietary Exposure Models

These models were developed to address the needs of the Office of Pesticide Programs for estimates of the distribution of acute exposures to pesticides from the consumption of dietary residues. The models are usually probabilistic. Unlike the dietary models in the site-specific software, these dietary models do not consider localized contamination of diet. In the future, these models may be superceded by aggregate exposure assessment software packages that include a dietary component.

Dietary Exposure Potential Model (DEPM)

The Dietary Exposure Potential Model (DEPM) has been developed by the EPA's Office of Research and Development via contract to Novigen Sciences and Environ Corp. (previously with Technical Assessment Systems, Inc.) over the past five years. The model is a combination of databases that compile information on dietary profiles—consumption of food groups defined from the USDA CSFII as well as the FDA's National Health and Nutrition Evaluation Survey. These are summary databases that simplify the use of the information with the functional tools in DEPM that link consumption to contaminant residue information. The model also contains recipe files that build a bridge to agricultural commodities. The entire model is available through the EPA website at www.epa.gov/nerlcwww/depm.htm , and the EPA's summary description of the model is presented below.

Dietary models can be used for identifying the importance of diet relative to other exposure pathways and indicating the potential for high exposure of certain populations. Existing consumption and contaminant residue databases, normally developed for purposes such as nutrition and regulatory monitoring, contain information to characterize dietary intake of environmental chemicals.

The model was developed for personal computers with the data files designed in dBASEIV® with FoxPro for Windows® applications programs for queries and reporting.

A model and database system, termed the Dietary Exposure Potential Model (DEPM), correlates extant food information in a format for estimating dietary exposure. The resident database system includes several national, government-sponsored food intake surveys and chemical residue monitoring programs. A special feature of the DEPM is the use of recipes developed specifically for exposure analysis that link consumption survey data for prepared foods to the chemical residue information, which is normally reported for raw food ingredients. Consumption in the model is based on 11 food groups containing approximately 800 exposure core food types, established from over 6500 common food items. The summary databases are aggregated in a fashion to allow analyst selection of demographic factors, such age/sex groups, geographical regions, ethnic groups and economic status. Daily intake is estimated by the model for over 300 pesticides and environmental contaminants. In addition, contributions to total exposure from exposure core food groups and individual exposure core foods can also be estimated.

The most recent version of the DEPM has evolved from a process that inventories available food consumption and food residue databases and integrates them in a format conducive for dietary exposure modeling. Several enhancements to the previous version (DEPM V2.3, available since 1996) have been made based on recommendations from exposure scientists. Briefly, the major modifications are:
Improved internal documentation;

- An integrated COMBINE tool, which allows the user to combine residue data from multiple residue databases for specified chemicals and foods;
- A USER-DEFINED DATA tool, which allows the user to incorporate foods or chemicals, and their residues and consumption data, that are not included in the resident databases;
- A TAP WATER option, which allows the user to estimate the contribution of tap water to daily dietary exposure; and
- Resident databases have been upgraded with several new chemicals, and USDA’s Pesticide Data Program (PDP) residue data and NHANES III consumption data have been added.

The residue databases available with DEPM V3.3.2 have not been significantly updated from those of DEPM V2.3. EPA is currently working on updating all of the resident databases to the most recent data available, and anticipates a release with updated data will be available within the year. In addition, a module will be added to allow users to import food diaries created by the user from Food Intake Analysis System (FIAS) software currently available for automatic coding of food items into the CSFII coding structure. Contact University of Texas, Human Nutrition

Center, by E-mail (hnc@utsph.sph.uth.tmc.edu) for availability of diary coding and nutrition analysis software.

Dietary Exposure and Evaluation Model (DEEM™)

The Dietary Exposure and Evaluation Model (DEEM™) is a proprietary software product created by Durango software and licensed by Novigen Sciences, Inc. The software is designed to estimate dietary exposures from pesticides used on agricultural commodities. DEEM™ also forms the dietary exposure component of the Calendex™ aggregate and cumulative assessment model. The details of the model were presented to the FIFRA Scientific Advisory Panel at the meeting of February 29 – March 3, 2000 (www.epa.gov/scipoly/sap/2000).

DEEM™ consists of four software modules: the main DEEM™ module, the Acute analysis module, the Chronic analysis module, and the RDFgen™ residue distribution module. The main module facilitates loading and editing chemical-specific residue files. RDFgen™ facilitates the residue distribution adjustments and creates summary statistics and residue distribution files based upon USDA or user-provided data. The Acute analysis and Chronic analysis modules provide dietary exposure assessment models based on USDA CSFII data together with recipe files (translation files) that convert residues in agricultural crops to residues in foods as consumed.

Three types of assessments can be generated with the models available in DEEM™: point estimate, simple distribution and probabilistic assessments using Monte Carlo techniques.

Data used by the model include:

- Demographic profiles of the individuals in the USDA CSFII from the 1989-1992 and the 1994-96 surveys. There is some public information that suggests that the model was enhanced by the addition of the Supplementary Children’s Survey of 1998. That survey was designed to augment the CSFII 1994-96 survey.

- Consumption data from the USDA CSFII studies, described above.

- Weighting factors developed by USDA for these studies. The dietary intake information collected by USDA involves having respondents keep a diary of their food consumption over three days (1989-91) or two non-contiguous days (1994-96). DEEM™ employs records from respondents that completed all days of their survey along with the weighting factors derived by USDA for those records. The weighting factors are designed to adjust the data for non-respondents, and allow combination of data from different years. The weighting factors are designed to make the overall survey records approximate a nationally representative sample of non-institutionalized persons residing in households in the US.

- Proprietary recipe files were initially used with the 1989-91 and 1994-96 CSFII data to convert residues in agricultural crops to residues in foods as eaten. Recently, the recipe files (now called translation files) devised by USDA have been incorporated into DEEM™ along with the 1998 Continuing Survey of Children containing additional demographic and consumption information for children.

- Processing Factors can be applied to the residues on crops as they pass from one form to another along the process of going from the farm to the plate. Processing can increase or decrease the concentration of the pesticide in food items. Default adjustment factors are included in DEEM™. The user may elect to use these data, their own data, or some combination as these files.

- Residue data of several types can be introduced into the model. Single points or distributions (whether empirical or parametric) may be used. Data may be employed representing residues at the point of use of the chemical in the field, or representing the foods at a later stage in the path from farm to plate

- Percent Crop Treated Information Not all chemicals are used on all crops all the time. Data describing the national uses of the chemical on a given crop or crop group may be used to refine the exposure estimate.

- Toxicity Estimates. Toxicity metrics are entered into the model by the user to be employed with the exposure assessment to represent risk. The traditional comparisons are employed: chronic dietary exposures are usually compared to the chronic reference doses (cancer potency factors, chronic NOELs, etc). The acute NOEL can be chosen to represent the toxicity for acute exposure (usually one day or a few days duration of exposure).

There are two types of dietary exposure modules.

The Chronic Module presents the average chronic exposure estimated on a per-capita consumption basis and is compared to the measure of toxicology from lifetime feeding studies. This module uses a point estimate derived for the total US population and 25 subpopulations. They are:

U.S. Population – 48 states, all seasons

Seasonal

U.S. –spring season
U.S.—summer season
U.S.—autumn season
U.S.—winter season

Regional

Northeast
Midwest

Southern
Western
Pacific Region (only in CSFII 89-91)

Ethnic
Hispanics
Non-Hispanic whites
Non-Hispanic blacks
Non-Hispanic other than black or white

Age and Gender
All infants < 1 year
Nursing infants < 1 year
Non-nursing infants < 1 year
Children 1-6 years
Children 7-12 years
Females 13+ pregnant/not nursing
Females 13+ nursing
Females 13-19 not pregnant, not nursing
Females 20+ not pregnant, not nursing
Females 13-50
Males 13-19
Males 20+ years
Seniors (55+)

The Chronic module uses a database of pre-calculated per-capita mean food consumption data (g/kg-bw/day) together with the residue data employed by the user.

The DEEM™ Acute Module computes exposure estimates for the total U.S. population, the subpopulations listed above, and six user-specified custom populations defined by age, gender, region, season, nursing status, race and ethnicity.

In this analysis, DEEM™ uses only those consumption records that show that the foods of interest were consumed by the respondent. Thus, these records reflect only those persons who could have been exposed because of their choice of foods are considered. The calculation then presents a file consisting of the entire per-user exposure distribution employing the USDA population weights or not. The DEEM™ acute module combines the food and food form consumption values for each individual in the population of interest with the residue value associated with the food or food form. If the user specified a distribution of residues, the Monte Carlo probability assessment is employed to combine a food consumption value for each individual in the population of interest with a randomly selected value from the distribution of residues.

Daily total exposures for each person are the sum of the exposures of all eating occasions for each person over the day. To express these exposures in terms of mg/kg BW, DEEM uses the body weight recorded on the CSFII record from which the consumption information was derived.

The Monte Carlo analysis performs a number of iterations (1000 are recommended by the designers), for each user-day. The data generated from these iterations are "binned" or summarized into frequency intervals to simplify the storing and sorting of these observations in subsequent exposure calculations.

LIFELINE™ AND CARES™

LifeLine™ Version 1.1 includes a dietary exposure module that can be used as a stand-alone dietary model. For additional information see the discussion in the aggregate models section of this report. CARES™ will also include a dietary module. LifeLine™ and CARES™ may be more available and transparent than DEEM™.

4. Aggregate Exposure Software

These models are being developed to address the need for aggregate exposure assessments as required by the Food Quality Protection Act (FQPA). All of the models use probabilistic approaches for characterizing exposure and address both dietary and residential exposures. However, these models do not address localized sources of dietary exposure, such as the effect of localized sources of contamination on backyard gardens, locally raised beef and dairy products, or fish in local bodies of water. Of the four models, two are still under development (CARES™ and SHEDS). The remaining two models Calendex™ and LifeLine™ are available from their developers.

CALENDEX™

Calendex™ is a software system developed by Durango Software and licensed through Novigen Sciences, Inc. The model is a proprietary product available under license. Access to the underlying algorithms, data structures, operations of the probabilistic functions and other key elements of the model are not available to non-license holders. However, limited information is available at the Novigen web site and in material presented to the EPA Science Advisory Panel[2].

The system provides estimates of exposures that are statistically representative of the U.S. population that occur from pesticide residues in food, in the home, and in tapwater. Calendex™ has a two-part structure, the first being the dietary analysis module, DEEM™ and the second part constructed to calculate the non-dietary component of the aggregate and risk.

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[2] Calendex™: Calendar-Based Dietary and Non-Dietary Aggregate and Cumulative Exposure Software System, Petersen et al. Novigen Sciences and Petersen, Durango Software. Documentation presented to FIFRA SAP, September 27, 2000. Source: www.epa.gov/scipoly/sap/2000/september/calendex. The developers participated in the International Life Sciences Institute (ILSI) workshops dedicated to the design of models for aggregate exposure assessment where many of the features of the models were discussed in detail (ILSI, 1997,1999). These concepts have also been presented, in whole or in part, at scientific meetings including the International Society for Exposure Assessment in October 2001.

In the non-dietary component of the model, the user supplies three types of data.

1. Use pattern information of pesticide products of interest with the frequency of application and amount of product applied;
2. Environmental concentration data on days before, during and after treatment (residue factors); and
3. Exposure factors such as body weight, breathing rate, and activity patterns (contact factors). These factors are supplied by the model and in some cases may be modified by the user.

Calendex™ contains information on a number of parameters utilized in the exposure analysis. The information is arranged in a series of "libraries" that can be used by the user to structure their analyses. The model utilizes the CSFII surveys conducted by USDA.

At the time of the September 2000 SAP review and documentation provided for that review, Calendex™ utilized data from the 1989-91 and 1994-96 surveys. Since that time, the 1998 USDA Supplemental Children's Survey was added to the database in the software. These data provide two important types of information. The first is a detailed diary of a person's diet during each of the two or three days of the survey. These data are used in the dietary assessment, described in the review of DEEM™. The second set of information is the demographic data collected as part of the survey. Each respondent was asked to provide data about their weight, height and information about their household income, education and factors that could influence dietary profiles. For children, the primary adult provided such information. Calendex™ stores selected demographic data in the CSFII Library. The data include respondents' ages, body weights and heights. The dietary intake information is used in the DEEM™ model.

The user of the software may create population subgroups based on gender, age, season, or region. Data in the CSFII library are binned accordingly for the analysis. If a non-dietary and dietary scenario are to be considered simultaneously, the user defines the demographics of interest at the initiation of the analysis and the DEEM™ module creates the dietary profile using both the demographic and food consumption components of the CSFII data. The demographic components from the dietary analysis are then linked to the non-dietary analysis by using matching demographic data (weight, height, etc) data from the model's CSFII library as necessary for the non-dietary component. In this way, the demographic profiles of a person considered in the dietary analysis are roughly equivalent to the demographic profiles for the non-dietary analysis to which it is pared. Details were not available to assess how the demographic equivalency is maintained when adding the drinking water component of the aggregate analysis. Since the demographic definitions for the estimates of water consumption provided in the EPA SOP's (which may be utilized in the assessment) may differ from those in the CSFII demographics, some problems of continuity seem possible.

Calendex™ uses either point estimates for the various parameters or distributions of the residues and other parameters in a Monte Carlo probability analysis. These distributions may reflect both uncertainty and variation. In both cases, residues in the medium are multiplied by the contact amount to determine the exposure estimate for this exposure route. In the dietary component, DEEM™, the analogous calculation is made: the residues in food are multiplied by the amount of the food consumed. This can be done for many people, using point estimates or using distributions of residues with distributions of contact amounts (or food consumed). Each exposure iteration can be repeated up to 5000 times for each participant in the CSFII survey records.

Four time periods of exposure duration are considered in Calendex™: daily/acute, short-term, intermediate-term, and chronic (up to one year). The user may specify the type of duration to be considered, guided by the toxicology information that suggests the duration of dosing that is required to elicit a specified biological effect. The basic unit for the model as presented to the SAP is total exposure/one day. Longer durations of exposure are computed by adding the daily exposures across the selected period of exposure and dividing by the number of days considered. This presents a time-weighted average across the chosen duration.

CUMULATIVE AND AGGREGATE RISK EVALUATION SYSTEM (CARES™)

CARES™ is being developed by the American Crop Protection Association with input from a variety of stakeholders. The purpose of the software is to determine aggregate risks from drinking water, residential and dietary exposure for a single pesticide and cumulative risks from pesticides that have a similar mechanism of toxicity. The software is currently under development. Based on announcement by the Group in July of this year, Version 1.0 of CARES™ will be undergoing testing late in 2001 and released to the public in 2002.

Because the software is still under development, it is difficult to specify the actual characteristics of the program. The following summary is based upon information obtained from the project's web page (http://alphacares.org/index.htm). Wherever possible, information from the most recent documents have been used. This information has been supplemented by information obtained from personal communications with CARES™ team members[3].

CARES™ is largely written in Visual Basic with parts written in C++. CARES™ will run in the Windows® environment. ACPA has stated that CARES™ will be available free of charge and will have open code that can be copied and modified without restriction. While CARES™ is designed as a stand-alone program, it is designed to be a module of the software program, **notitia**™, see below. Use of **notitia™** may be required when CARES™ is used to access industry databases.

Because CARES™ is intended to support regulatory decisionmaking; the model's focus is the general U.S. population. However, the output of the model will allow the user to separately evaluate risks by subpopulations defined by age/gender, Race/ethnicity, and geographical region. These subpopulations include:

Age/gender:

Male and Female Infants <1 year
Male and Female Children 1-3 years

[3] Personal communications with Muhilan Pandian on the topics of model design, platform, and relationship between CARES™ and notita™.

Male and Female Children 4-6 years
Male and Female Children 7-12 years
Male Teens 13-19 years
Female Teens 13-19 years
Male Adults 20-54 years
Female Adults 20-54 years
Male and Female Adults >55

Race/ethnicity:
White
Black
Asian
Native American
Hispanic
Other

Regions and Sub-regions:
- Northeast
  - New England
  - Middle Atlantic
- Midwest
  - East North Central
  - West North Central
- South
  - South Atlantic
  - East South Central
  - West South Central
- West
  - Mountain
  - Pacific

Due to the approach used, the user may not be able to investigate risks by more than one of the categories. Thus, analyses by region and age group, or age group and Race/ethnicity may not be permitted.

The CARES™ project has developed a novel approach for characterizing interindividual variation. This approach creates a "Reference Population". This population is defined by sampling the Public Use Microdata Sample (PUMS) of the 1990 U.S. census (Census, 1992). The Reference Population consists of 100,000 individuals. The individual have been selected to match the US population (as measured by the 1990 Census). The number of 100,000 was selected as being sufficiently large to allow a minimum of 5,000 individuals in each of the above subpopulations. (However, combinations of classes Race/ethnicity and Age/gender may or may not meet the criteria of 5,000 individuals).

These data are used to establish what is called a vector of individual characteristics (VIC). The VIC consists of values that never change, the VIC Kernel, and portions that change VIC

Augmentation. The VIC Kernel is composed of data from the census called “real data” and data from other surveys, which is called “attributed data”. The CARES™ project then uses the “real data” in the VIC to select “attributed data” on the individual’s physiology and food consumption. Physiology data is selected from one of the 21,269 individuals in the 94-98 CSFII. This selection of data was performed by matching a person’s record in the Census data with a person’s record in the CSFII.

The characteristics of the home necessary for residential exposure assessment are only partially provided by the census records. Therefore, the VIC Kernel will need to be matched to other databases of residential characteristics. As of the drafting of the CARES™ white paper of March 15, 2001, the details of this process had not been finalized. However, it is clear that CARES™ will be tracking different microenvironments in the home, such as indoors, turf, gardens, pets, ornamentals, and pools. Because of the short period of duration, the model does not allow the modeled individuals to live in more than one house. Thus, residential mobility is not considered.

The design of CARES™ is being closely linked to a number of industry-sponsored datasets. The Outdoor Residential Exposure Task Force (ORETF) has developed survey information on residential use and application of outdoor pesticides in the Outdoor Lawn & Ornamental Product Use Survey. A second data set is the Residential Exposure Joint Venture (REJV) survey of pesticide product use. A 3-month pilot study has been completed with a sub-sample of U.S. households to evaluate the survey instrument for use in a 12-month (one calendar year) survey. The primary purpose of the survey is to obtain the necessary information regarding the timing and frequency of product use events (and related ancillary information) to permit more realistic calendar-based aggregate and cumulative exposure modeling. The survey is currently ongoing and its initial phase will be completed in 2002. The results of these survey’s are being organized in notita™.

The CARES™ team has not released information on the design of the tapwater portions of the model. However, the team is attempting to link groundwater and surface water models such as SIGROW, PRZM/EXAMS, and GENEEC and geographic information on pesticide residues into CARES™. The model may also attempt to consider the impact of water treatment on residues. Data on tapwater consumption rates will be taken from the CSFII study.

The basic unit of exposure in CARES™ appears to be a single day. Each day’s exposure is determined by summing the doses that occur from a series of events that occur during the day. These events include meals, tapwater consumption, and residential exposure to the residues from specific microenvironments. These events may be of a few hours or minutes duration. While each event’s route-specific exposures and doses are determined individually by the model, the exposures are summed to produce estimates of daily exposures the end of the simulation of each day. Thus, the shortest period evaluated in the model’s output is a single day. The software allows the user to track the average dose that occurs over any number of days from 1 to 365 days. CARES™ limits its simulation of individuals’ lives to a period of one year. The year is defined as beginning with each simulated individual’s birthday and proceeding for 365 days. Each day is tracked in terms of the day of the week and the season of the year. The dates of birthdays are randomly assigned different calendar dates based on data taken from the CSFII.

CARES™ is constructed to support EPA and the regulated community in meeting the requirements of the FQPA. The FQPA specifies that EPA will determine the aggregate and cumulative risks associated with pesticides used on agricultural products and in residential environments. The exposures to pesticides used on agricultural products will also consider tapwater exposures. As a result, the model focuses on exposures to pesticide residues in food, tapwater, and in residential environments.

CARES™ dietary module accepts data on contaminants that occur in agricultural commodities this approach is shared by the DEEM™/Calendex™ and LifeLine™ Model. The process begins by pulling a dietary record from USDA's CSFII. This record specifies the specific food items and amounts of the items consumed by the individual. The distribution of residues in each of the food items is modeled based on the distribution of contaminant levels in the commodities used in the recipe for a food item and the amount of the item an individual consumes. The total oral dose for a given day is determined by summing the dose from each food item consumed on a day. CARES™ intends to use the 1994-1996, 1998 CSFII, with the FCID recipe files (referred to the as translation files) developed by USDA.

As discussed above, CARES™ determines exposure to contaminants in water supplies that occurs by direct ingestion. Based on information released by the CARES team, the model will not consider exposures from non-ingestion pathways (dermal contact and inhalation during showering).

The approach for residential exposures in CARES™ is built around the exposure scenarios and the resulting exposure/dose equations given in EPA's Residential SOPs (EPA 1997, 1999, and 2001). Details provided by the user on each product are used to estimate residue levels for:

- Pesticides on the surfaces of indoor microenvironments;
- Pesticide levels in air; and
- Pesticide levels on turf and in soil (for pesticides used out of doors).

The user is also required to enter data on the frequency of use of the pesticide and how the use will vary by time of the year, day of the week, and the fraction of homes that will use the product. This data is used in a port of the program called an event generator. The event generator uses an annual frequency of use and the correlations with seasons and days of the week to generate a synthetic history of usage of the product. CARES™ will also allow the use of the results of the REJV survey when it becomes available.

LIFELINE™

The LifeLine™ Model Version 1.1 (LifeLine™) was created by The LifeLine Group[4] (LLG) a nonprofit organization created "to advance scientific knowledge in the field of toxic chemicals." LifeLine™ is an ongoing project with versions 1.2 and 1.3 under development. Version 1.1 is currently available. Individual licenses are available with out charge from the LLG.

[4] LLG is the primary contractor for this report.

LifeLine™ was created as a tool for the assessment of aggregate and cumulative exposures to pesticides in support of the regulatory decisionmaking under FQPA (Price et al. 2001). The model addresses exposures that occur from the use of pesticides on agricultural crops, in residences (homes and yards), and pesticide residues that occur in water supplies. The model determines the aggregate and cumulative doses that occur from these exposures and the risks associated with such doses. LifeLine™ seeks to model the interindividual variability and the longitudinal intra individual variability of the individuals that make up the U.S. population. Because the model was intended to support regulatory decisionmaking, the model's focus is the general U.S. population and subgroups defined by gender, race, income, ethnicity, region of the U.S., season of the year, and the age of the individual.

The model can be used to characterize exposures to the active and inert ingredients of pesticides used on a variety of agricultural commodities. The model can also be used to evaluate any substance in the food or tapwater where the levels of contamination can be specified in different agricultural commodities or tapwater supplies.

LifeLine is written entirely in C++ and is a stand-alone program that runs on Windows® 95 Windows® 98 and Windows® NT and Windows® ME. Outputs from the model can be evaluated using database programs such as dbase®, Access, and Excel.

LifeLine™ models longitudinal variation of individuals over their lifetimes starting with the characteristics of the individuals at birth. LifeLine™ begins the modeling of individuals' birth characteristics based on data taken from the National Center for Health Statistics (NCHS) Public-use - database of birth records for 1996. These records are used to determine the permanent characteristics of the individual. Once the characteristics of the individual are established, this data is used to guide the simulation of the physiological characteristics of the person throughout his or her life and the number and individual characteristics of the homes she or he will reside in during the simulated life.

Physiological characteristics are based on longitudinal models of growth developed using nationally representative data collected in the Third National Health and Nutrition Examination Survey (NHANES III).

Residential characteristics of the individuals' homes are modeled in two steps. First, the residential mobility of the individuals is modeled to determine the type, setting, and region of each home the individual will reside during his or her lifetime. This modeling is performed using data from the Current Population Statistics, U.S. Census. Based on the type of home and the individual's SES, a record from the American Housing Survey is selected and used to describe the characteristics of the home (type and number of rooms, lot size, finished floor space). These data are used with a data set on relative room sizes developed by the LifeLine Group and published values for whole house exchange rates.

Finally, the data on the age, season, and gender are used to select the data on dietary consumption and data on age, gender, region, season, and day of the week (a weekend day or weekday) are used to select a record from the National Human Activity Pattern Survey (NHAPS).

The basic unit of exposure in LifeLine™ is a single day. Each day's exposure is determined by summing the doses that occur from a series of events that occur during the day. These events include meals, tapwater consumption, and activities occurring in specific microenvironments. These events may be of a few hours or minutes duration.

While each event's route specific exposures are determined individually by the model, the exposures are summed to produce estimates of daily exposures at the end of the simulation of each day. Thus, the shortest period evaluated in the model's output is a single day.

The software allows the user to track the average dose that occurs over any number of days from 1 to 365 days. In addition, seasonal, and annual doses are tracked for each year of an individual's life. Finally, lifetime average doses can be determined for each individual.

LifeLine™ Version 1.1 assesses exposures to pesticide residues in food, tapwater, and in residential environments. While pesticides are the focus of LifeLine™, the model can be applied to a material where the distribution of residues can be specified to occur in specific agricultural products (specific fruits, meets, grains, etc.) or to any material where the distribution of residues in tapwater can be specified.

LifeLine™ Version 1.1 allows the user to calculate dietary exposures using either of two versions of the CSFII. The user may select the 1989-1991 CSFII, with associated food recipe files. Version 1.1 also, however, allows the user to select the 1994-1996, 1998 CSFII, with associated recipe files (referred to as translation files) developed by EPA and USDA.

Version 1.1 of LifeLine™ determines exposure to contaminants in water supplies that occurs by direct ingestion, dermal contact during showering, and inhalation during showering. The user is allowed to specify the range of contamination as a function of season, region, source of water, and setting (urban/suburban versus rural). Tapwater consumption can be based on data from the CSFII surveys or from age specific defaults. Estimates of dermal and inhalation exposure are based on EPA models of diffusion from dilute solutions, and showering models.

Version 1.1 of LifeLine™ assesses exposures to pesticides that occur from the treatment of residential pest by the homeowner or by professional pest controllers. The model begins by focusing on pest pressures (the probability that a specific pest will require control on a residence). Based on a residence's pest pressures, the model simulates the probability that a specific pesticide product is used on a given day in one or more microenvironments. Details provided by the user on each product are used to estimate residue levels for:

- Pesticides on the surfaces of indoor microenvironments;
- Pesticide levels in air; and
- Pesticide levels on turf and in soil (for pesticides used out of doors).

Once the process is completed, data on individuals' activities are used to define the interaction of the individual with the residues in a specific microenvironment. These interactions include:

- Inhalation of air containing pesticide residues;
- Dermal contact with hard surfaces (hard floors);

- Dermal contact with soft surfaces (carpet);
- Dermal contact with turf;
- Oral exposures from mouthing events; and
- Incidental consumption of soil and grass.

Stochastic Human Exposure and Dose Simulation (SHEDS)

SHEDS is part of EPA's National Exposure Research Laboratory's (NERL) research program to develop probabilistic human exposure source-to-dose human exposure (HES2D) models that estimate multimedia and multipathway pollutant exposures of general as well as at-risk populations. The HES2D is being designed to predict and diagnose complex relationships between pollutant sources and dose received by different population sub-groups, e.g. children and the elderly. HES2D incorporates models, databases, and analytical tools within an integrated modeling framework. The methods and models developed under this research program will provide estimates of variability and uncertainty in the predicted exposure distributions and characterize factors influencing high-end exposures. These models will address both aggregate (all sources, routes, and pathways for single chemical) and cumulative (aggregate for multiple chemicals) exposures.

SHEDS is a model in development. The initial generation of the pesticide version of the model has been circulated inside EPA but has not been publicly released. No announcement has been made on the schedule for release. The model is currently scheduled for review in mid-2002 by the Office of Pesticide Program's Science Advisory Panel. The initial and second generations of SHEDS-Pesticide are constructed in SAS and are intended to run on the PC.

First-generation versions of SHEDS models have been developed for particulate matter (PM) and pesticides. The particulate matter version SHEDS-PM is designed to work in conjunction with MENTOR. SHEDS-PM is collaboration between NERL scientists and external scientists from Environmental and Occupational Health Sciences Institute (EOHSI) and Lawrence Berkeley National Laboratory (LBNL).

The SHEDS model for pesticides (SHEDS-Pesticides) is being developed in stages. The first generation SHEDS-Pesticides focused on children's exposure and absorption on a single day post-pesticide application via dermal contact with and non-dietary ingestion of surface residues in and around the home. It also allows for characterization of uncertainty as well as variability in predicted population estimates of exposure and dose. The algorithms for dermal exposure and the temporal framework for SHEDS-Pesticides were initially developed as the doctoral thesis of Dr. Valerie Zartarian and is part of the Stanford University model DERM (Zartarian, et al. 2000).

The second-generation SHEDS-Pesticides extends the first generation model by including the inhalation and dietary ingestion routes in addition to dermal contact and non-dietary ingestion. The algorithms used to estimate exposure via the various routes and pathways will been refined. The refined model is intended to simulate an individual's exposure for periods up to one year.

As a model in development, decisions on the target population have not been finalized. However, the goal of SHEDS-Pesticides is to define pesticide exposure to the general population. SHEDS-Pesticides uses a microactivity approach to estimating dermal exposure. This data is dependent on videotaped data on hand and object to mouth behavior. Currently such data is limited to children. Thus, the initial version of SHEDS is limited to the ages where videotaped data is available. This limitation may be removed in future versions.

SHEDS-PM is integrated with MENTOR. MENTOR is a geographically based model that included data on the location of individuals through out the U.S. by census tract. Thus, the model can focus on any subpopulation defined down to census tract. Based on the demographic data for the census tract the model can identify the number of residents in each census tract that fall into various age and gender categories.

The initial version of SHEDS-Pesticides determines the total dose for periods up to a single day. SHEDS-Pesticides is being revised to model periods with durations of up to one year. Details of the approach used in this longitudinal modeling have not been released.

The initial version of SHEDS-Pesticides is limited to pesticides and other dislodgeable compounds present on surfaces in residential compartments. SHEDS-PM is limited to airborne levels of particulates. The sources of particulates are indoor sources, ambient sources, and smoking. Residential exposures considered in the initial version SHEDS-Pesticides are limited to dermal exposure and oral exposures from incidental hand-to-mouth and object-to-mouth. The initial version of SHEDS relied on NHAPS to define the location of the individual in the microenvironments. Data on the distribution of residues on surfaces is supplied by the user.

Dermal algorithms taken from the DERM model developed to investigate dermal and oral exposure to residues on surfaces (Zartarian et al. 2000). The modeling approach defines a child's exposure in terms of a series of compartments. These include:

- Surfaces
    - At the site of application of pesticide;
    - Near the site of application of pesticide; and
    - Far from the site of application of pesticide.
- Objects
- Skin
    - Hand
    - Reminder of the body
- Mouth

The pesticide residue is modeled as entering or leaving these compartments. Pesticide residues move into the skin compartments during contact events. The amount transferred is a function of the amount of dislodgeable residue on the surface, the transfer efficiency of each contact, and the area of contact. The values of each of these factors are assumed to be both variable and uncertain. The dermal and oral doses are determined based on the mass entering the mouth as the result of contaminated hand or object entering the mouth (oral dose) and the time weighted average of the mass of residues on the skin and an absorption rate (Zartarian et al, 2000). The data on macro activities is taken from the CHADS. All remaining information must be supplied by the user.

SHED-Pesticides along with TRIM (see below) are the only modeling programs that have proposed to separately investigate both uncertainty and variability. SHEDS model used the 2-D Monte Carlo modeling (Hoffman and Hammonds, 1994; Price et al. 1996; Zartarian et al. 2000) to define the variability in dose in the simulated population and the uncertainty in the estimates. The sources of uncertainty addressed in the initial version of SHED-pesticides are limited to parameter uncertainty.

5. Libraries of Models and/or Datasets

The software packages are collections of smaller models or data sets relevant to characterizing worker exposures, the release, fate and transport of chemicals through the environment. In several cases, the models offer an overarching framework for use of individual models.

CHEMSTEER

The United States Environmental Protection Agency, Office of Pollution Prevention and Toxics' (OPPT) Chemical Screening Tool for Exposures and Environmental Releases (ChemSTEER) is a personal computer-based software program that uses OPPT's most current screening-level workplace exposure and release assessment methods. ChemSTEER generates screening-level estimates of environmental releases of and worker exposures to a chemical manufactured and used in industrial and commercial operations and workplaces. The tool also contains data and estimation methods to assess situations involving common industrial / commercial sectors (e.g., industrial laundries) and chemical functional uses (e.g., surfactant in hard surface cleaner). ChemSTEER is distributed in a downloadable file from EPA's Internet site.

EML/IMES

The United States Environmental Protection Agency, Office of Research and Development created the Exposure Models Library. EML is distributed as a CD-ROM and is comprised of over 120 model programs that can be used for transport modeling and exposure assessments. The model files may contain source and/or executable code, sample input files, and other data files, sample output files, and in many cases, model documentation in WordPerfect, ASCII text, or other similar formats. The integrated model evaluation system is used to assist in selecting the appropriate models, provide literature citations on model validations, and demonstrates model uncertainty protocols.

PC-GEMS/RISK-PRO

Personal Computer-Graphical Exposure Modeling System provides access to single-medium and multimedia fate and exposure models, physical and chemical properties estimation techniques, statistical analysis, graphics, and mapping programs with related data on environments, sources, receptors, and populations. The environmental models in PC-GEMS are atmospheric, surface water, land unsaturated (soil) and saturated (groundwater) zones, and multimedia in nature. It is available with air, surface water and ground water models and associated environmental and 1980 population data encompassing most of the U.S. RISK-PRO is an updated, user-friendly version of PC-GEMS produced by General Sciences Corporation (GSC).

Modeling ENvironment for Total Risk Assessment (MENTOR)

MENTOR is an ongoing modeling project of the Computational Chemodynamics Laboratory of the Environmental and Occupational Health Sciences Institute (jointly sponsored by the Robert Wood Johnson Medical School and Rutgers University).

MENTOR is not a single model; it is an evolving, open, environment for supporting consistent multiscale source-to-dose modeling for human exposures to contaminants. MENTOR has a modular structure with a geographic interface and incorporates (a) libraries of environmental and biological process models (macroenvironmental, ecological/food-web, local multimedia, microenvironmental, activity pattern/exposure event, biological fate and transport, and dose response modules), and (b) libraries of tools to support integrated probabilistic and diagnostic analyses.

The long term goal of MENTOR is to provide state-of-the-art tools for studying the complex and multiscale phenomena that may need to be quantified in order to develop effective control and intervention strategies. Currently the MENTOR project is in a research mode and there are no immediate plans to release a version of the software for general use. However, MENTOR will eventually provide an extensible set of ready-to-use methodological tools for performing assessments of exposure/dose for populations or specific individuals, and for a variety of user-defined scenarios.

MENTOR is a Unix program. Individual programs in the MENTOR framework are written in a variety of programming languages. MENTOR is intended to run on high end PCs.

MENTOR is designing and constructed as a series of models and integrated data bases that will allow the modeling of regional and local sources of atmospheric contaminants (ozone, particulates, and other contaminants), groundwater contamination, indoor airborne contaminants in the residential and occupational environments, exposure that occur as a result point source and non-point source discharges. The goal of MENTOR is to establish a consistent and integrated geographical and temporal framework for multimedia release, fate and transport. As discussed above, MENTOR is linked to the SHEDS model. In this case, SHEDS-PM is viewed as a sub module under the MENTOR system.

MENTOR is not designed to model a specific population. Under MENTOR the modeled population can be defined in a wide variety of ways using geographical and demographic criteria.

The various components of Mentor deal with a wide variety of time frames. Periods greater than a year may be considered in ground water models or models of long-term changes in climate. SHEDS-PM in the MENTOR system considers exposure events with durations of five seconds to one year. Indoor air models using computational fluid dynamics may model the movement of contaminants over shorter periods of time.

MENTOR has a strong orientation towards the exposure that occur as a result of the movement of contaminates in the environment (national and region air quality, local air quality, widespread or localized contamination ground water.) However, the model framework could be applied to any source of contaminant. The MENTOR approach lends itself to compartmental and mechanistic based models of exposure. These approaches can be based on either macro or microactivity approaches.

Total Human Exposure Risk database and Advanced Simulation Environment (THERdbASE)

THERdbASE was developed by USEPA's Office of Research and Development (National Exposure Research Laboratory, Las Vegas). THERdbASE is a PC-based computer modeling and database system that contains exposure and risk related information. The system provides a framework for the construction of a suite of exposure- and risk-related models within the Modeling Engine by using information available in data files within the Database Engine. THERdbASE provided a common basis for conducting all residential exposure assessments. THERdbASE married an array of data files with a suite of indoor and outdoor residential and ambient models, and permitted a "cafeteria" approach to selection of data file subsets and models for accomplishing specific modeling activities. Data files included demographic data, food consumption data, physiological data (e.g., distributional data on inhalation rates and body weights), monitoring data on pesticides, and other useful information.

notita™

notita™ is PC-based data model management software[5] written in Visual Basic. notita™ combines elements of database management, spreadsheet, and statistical analysis software. The model also facilitates simulation programs created under the notitia™ framework. notita™ allows the management of quantitative information that is linked to qualitative information call attributes. Examples of attributes associated with scientific data include specific characterization (e.g., mass and force) and units (e.g., kg and Newton). The ability of a single program to deal with models and data provides a single integrated environment that facilitates the use and management of data and models in an integrated environment.

[5] All information on notita™ is take from the infoscience.com webpage or from personal communications with Dr. Muhilan Pandian.

notitia™ is a user-friendly, graphical, icon-based, modular, Microsoft Windows® software designed by using object-oriented principles. The program is written in Visual Basic.

4.0 Evaluation of the Software Packages

In the Conceptual Framework for a Tiered Evaluation of Children's Health 65 Fed Reg 81709 (December 26, 2000), information on exposure is used at four different points, the initial qualitative assessment, the baseline conservative (or screening) assessment, the refined exposure assessment, and a detailed chemical-specific monitoring program. The *initial qualitative assessment* is a determination of whether a chemical will occur in the media with which a child will come in contact. As discussed above, these media include:

1. Chemicals present in food, tapwater, or breast milk;
2. Chemicals present in the soils or vegetation (grass or leaves) around residences and institutions (schools and day-care);
3. Chemicals present on surfaces (floors, accessible surfaces of furniture, toys, clothing, and bedding); and
4. Chemicals present in indoor air (from both local and distant sources).

The initial qualitative assessment will focus on a determination of whether the chemical is likely to be present in any of the above media. This assessment will be based on the use, release, and environmental fate of the chemical. For example, if a chemical is only used as a captive intermediate and rapidly breaks down in the environment, then the potential to occur in any of the above media will be small. In contrast, a compound that is used as a solvent in a number of consumer products would be considered to have a much greater potential to occur in indoor air and on indoor surfaces.

Certain software could be useful in this initial assessment. Models of release estimation and environmental fate and transport could assist in the determination of whether environmental releases could result in contamination of local food supplies (E-FAST, CalTOX, and RiskPRO), drinking water wells (API DSS, MEPAS, and CalTOX) and outdoor air (TOXST/TOXLT).

The *conservative, or screening exposure assessment,* seeks to separate out those chemicals in which there are sufficient data to conclude that children, if exposed, are unlikely to receive a dose of toxicological concern. Unlike the initial qualitative assessment, this stage of the tiered approach will require an actual estimate of dose. The estimate of dose will typically be conservative and will rely on conservative "default" assumptions. The assessment is likely to take place in two stages, an initial determination of the specific medium or media where the chemical can be expected to occur and the development of dose estimates that occur from the child's exposure to the effected medium or media.

For software to be useful in the evaluation of exposure to children, the program must have the ability to characterize exposures for the four media listed above. Table 1, presents a breakdown of the routes of exposure addressed by each of the packages. As the Table indicates, none of the software packages addresses all of the relevant routes of exposure. This suggests that the choice of software may be a function of the media and routes of exposure that are relevant to the chemical. For example, if the chemical is non-volatile, the software for indoor air modeling (CONTAM, MCCEM, RISK, and IXAQ) will not be useful. Chemicals that occur in the general food supply may require one of the dietary software packages (LifeLine™, CARES™, or DEEM™).

In general, the most useful types of models are the dietary aggregate exposure assessment software (CARES™, Calendex™, and LifeLine™), consumer product software (CONSEXPO and E-FAST), and site-related software packages (CalTOX). All three types of software address exposures that occur by multiple pathways to the same individual. Many the packages allow consideration of complex temporal and spatial patterns of exposure and permit the use of probabilistic models. However, most of the consumer product and site-related models do not address general dietary exposures. More importantly, the consumer product and site-related models tend to focus on exposures as a function of a single source (plasticizers in children's toys or contaminates in the soil of an industrial site). As a result, they may not be sufficiently flexible to characterize multi-source exposures to children.

The aggregate software packages currently available or under development are intended to characterize both multipathway and multisource exposures. However, CARES™ and SHEDS are still under development and Calendex™ has not been made generally available. Thus LifeLine™ may be the most available program. Neither of the aggregate programs address the breast milk pathway or localized food contamination. In addition, only LifeLine™ will characterize variation in long-term exposures (greater than one year).

The software packages used in the *refined exposure assessment* will require the ability to modify defaults, incorporate different types of information on variability, and model variability and uncertainty in dose. Software packages such as E-FAST, or RISK*ASSISTANT (or the residential SOPs) are not able to perform these tasks. The software that should be considered for this purpose will be the aggregate software (CARES™, Calendex™, and LifeLine™), CalTOX, and CONSEXPO. All of these models have the ability to model variability and or uncertainty in exposure.

Where the conservative assessment has eliminated all but one source or pathway, certain software packages may be useful for the refined assessment. For example, if inhalation from consumer products is the only pathway of concern then MCCEM may be useful. If the chemical is used as a solvent, then PROMISE may be useful. TEM will be useful for the evaluation of volatile chemicals that occur in drinking water since it tracks dermal, oral, and inhalation exposures.

The final type of exposure assessment in the Framework is the Detailed Exposure Assessment (Monitoring). Monitoring data has different strengths and weaknesses then data from modeling (EPA, 1992). Monitoring can allow a direct conformation of modeling predictions. However, many exposures of interest cannot be modeled directly. For example, if a chemical has no current exposures, then monitoring is not possible. Monitoring over long periods of time (months or years) is not feasible; thus, estimates of chronic exposure typically cannot be based upon monitoring data.

Many researchers have advocated a combination of monitoring and modeling. Where the monitoring provides conformation of the models' predictions and the models extend the findings of the monitoring study to address exposures of interest to the risk manager. Therefore, exposure software used in the refined exposure assessments may also be useful in the detailed exposure assessment.

5.0 Abbreviations used in this Report

@Risk™
An Excel add on program that allow the user to perform Monte Carlo Analysis

ACPA American Crop Protection Association
Recently renamed CropLife America

ADC Average Daily Concentration

ADD Average Daily Dose

APDR Acute Potential Dose Rate

APEX Air Pollution EXposure
An indirect exposure model –part of TRIM

API DSS American Petroleum Institute Decision Support System
Software for waste sites

AWWARF American Water Works Association Research Foundation

BEAM Benzene Exposure Assessment Model
An indirect exposure model

C, C+, C++
Programming languages

CalTOX
Software for waste sites or local source of environmental releases

CARES™ Cumulative and Aggregate Risk Evaluation System
Aggregate software developed by CropLife America

CHAD Consolidated Human Activities Database

ChemSTEER Chemical Screening Tool for Exposures and Environmental Releases

CMFM Completely Mixed Flow Models

CONSEXPO-3 CONsumer EXPOsure Model
Software to assess exposure and risk from consumer products

Cpeak Peak Indoor Air Concentration

CPIEM California Population Indoor Exposure Model
An indoor air exposure model

Crystal Ball™
Excel add on program that allow the user to perform Monte Carlo Analysis

CSFII Continuing Survey of Food Intake by Individuals
Major survey of US dietary patterns performed by USDA

DEEM™ Dietary Exposure and Evaluation Model
Dietary software

DEPM Dietary Exposure Potential Model
Dietary software

DERM
A model of dermal absorption developed at Stanford University

DERMAL
Exposure model superceded by E-FAST

DISGEN© DIStribution GENerator
Software for performing Monte Carlo

E-FAST Exposure and Fate Assessment Screening Tool
Software to assess exposures from local releases to air water and groundwater and from consumer products, developed by EPA.

EOHSI Environmental and Occupational Health Sciences Institute

EML Exposure Models Library

ERDEM Exposure Related Dose Estimating Mode

EUSES European Union System for the Evaluation of Substances
Software to assess exposures from local releases to air water and groundwater and from consumer products developed by EPA

Facsearch
Exposure model superceded by E-FAST

FCID Food Commodity Intake Database

FIAS Food Intake Analysis System

FIFRA Federal Insecticide Fungicide Rodenticide Act

FLUSH
Exposure model superceded by E-FAST

FQPA Food Quality Protection Act

GENEEC
A ground water model

HAPEM Hazardous Air Pollutant Exposure Model
An indirect exposure model

HEM Human Exposure Model
An indirect exposure model

HES2D Human Exposure Source-to-Dose

IXAQ
Simulation Tool Kit for Indoor Air Quality and Inhalation Exposure

LADC Average Daily Concentration

LADD Lifetime Average Daily Dose

LBNL Lawrence Berkeley National Laboratory

LLG The LifeLine Group
Nonprofit firm created to develop software

MAVRIQ Model for the Analysis of Volatiles and Indoor Air Quality
Early indoor air model superceded by TEM

MCCEM Multi-Chamber Concentration and Exposure Model
Indoor air model

MENTOR <u>M</u>odeling <u>EN</u>vironment for <u>T</u>otal <u>R</u>isk <u>A</u>ssessment
A modeling environment developed for model research

MEPAS Multimedia environmental pollutant assessment system
Software for waste sites or local source of environmental releases

NCHS National Center for Health Statistics

NHANES-III Third National Health and Nutrition Examination Survey

NERL National Exposure Research Laboratory's

NHAPS National Human Activity Pattern Survey

NIST National Institute of Standards and Technology

OPPT Office of Pollution Protection and Toxics

ORETF Outdoor Residential Exposure Task Force

PBPK Model Physiologically Based Pharmacokinetic model

PC-GEMS Personal Computer-Graphical Exposure Modeling System

PDM3
Exposure model superceded by E-FAST

pHAP probabilistic Hazardous Air Pollutant exposure model
An indirect exposure model

pNEM probabilistic NAAQS Exposure Model
An indirect exposure model

PROMISE© Probabilistic Methodology for Improving Solvent Exposure Assessments
Exposure software for solvents and products containing solvents

PRZM/EXAMS
A ground water model

PUMS Public Use Microdata Sample
Publicly available portion of the US Census

RECS Residential Energy Consumption Survey

REUWS Residential End Uses of Water Study

REJV Residential Exposure Joint Venture

SAP EPA Science Advisory Panel
Panel created under FIFRA to advise EPA on scientific issues.

RME Reasonable Maximum Exposure

SCREAM South Coast Risk and Exposure Assessment Model
An indirect exposure model

SCIES
Exposure model superceded by E-FAST

SEAS
Exposure model superceded by E-FAST

SES Socio-Economic Status

SHAPE Simulation of Human Activities and Pollutant Exposure
An indirect exposure model

SHEDS Stochastic Human Exposure and Dose Simulation
An indirect exposure model

SIGROW
A ground water model

SKINPERM
A dermal absorption model that is part of CONSEXPO-3

TEM Total Exposure Model
Indoor Air model

THERdbASE Total Human Exposure Risk database and Advanced Simulation Environment

TRIM Total Risk Integrated Methodology

TOXLT Toxic Modeling System Long-Term

TOXST Toxic Modeling System Short-Term

QuickBASIC® for the DOS
Programming language

VIC Vector of Individual Characteristics
Portion of CARES that provides internally consistent definition of the modeled individuals

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